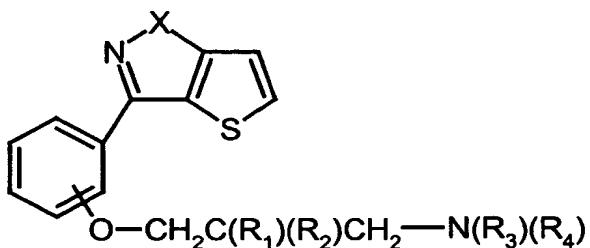


### **What is claimed is:**

### **1. A compound of Formula I :**



### Formula I

5 a pharmaceutically acceptable salt or stereoisomer thereof,

wherein

X is N(CH<sub>3</sub>) or O;

R<sub>1</sub> is OH or C<sub>1-6</sub> alkoxy;

R<sub>2</sub> is H or C<sub>1-6</sub> alkyl;

10 R<sub>3</sub> is (CH<sub>2</sub>)<sub>n</sub> Q, CH<sub>2</sub>CH(OH)Q, CH(CH<sub>3</sub>)Q, 1,2,3,4-tetrahydronaphthyl, indanyl, or adamanyl, wherein

**Q** is thienyl, phenyl, furanyl, naphthyl, pyridyl, indolyl, indazolyl, cyclohexyl, 1,2-methylenedioxyphenyl, cyclohexenyl, 1H-pyrazolo[4,3-*c*]pyridyl, and

15 Q is optionally substituted with one or two moieties independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, hydroxy, S(O)<sub>2</sub>NH<sub>2</sub>, trifluoromethyl, or cyano, and

n is 1 or 2;

20 R<sub>4</sub> is H or C<sub>1-6</sub> alkyl; or

$R_3$  and  $R_4$ , together with the nitrogen atom to which  $R_3$  and  $R_4$  are attached, form 1,4-dioxa-8-azo-spiro[4.5]decanyl, piperazinyl, morpholinyl, piperidinyl, pyrrolidinyl, azocanyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydro- $\beta$ -carbolinyl, 4,5,6,7-tetrahydrothienyl[3,2-c]pyridyl, or 8-aza-bicyclo[3.2.1.]octane, each of which may be mono- or independently di-substituted with halo,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy,  $C(O)phenyl$ , OH, CN, O-phenyl or  $(CH_2)_mZ$ ,

Z is benzisoxazolyl, indazolyl, benzisothiazolyl, benzothienyl, pyrimidinyl, pyridyl, 1,2-methylenedioxyphenyl, or phenyl, and

5

Z, CH(OH)phenyl or O-phenyl are optionally substituted with one or two moieties independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, hydroxy, trifluoromethyl, S(O)<sub>2</sub>NH<sub>2</sub>, or cyano, and

10

m is 0 or 1;

provided that when R<sub>1</sub> is OH, R<sub>2</sub> is H:

- (1) R<sub>4</sub> is H, and R<sub>3</sub> is (CH<sub>2</sub>)<sub>n</sub>Q, where n is 1 or 2, then Q cannot be indolyl or phenyl; or
  - (2) R<sub>3</sub> and R<sub>4</sub> form piperazinyl substituted with (CH<sub>2</sub>)<sub>m</sub>Z, when m is 1, then Z cannot be phenyl.
2. A compound according to claim 1 wherein  
Q is thienyl or pyridyl;  
or R<sub>3</sub> and R<sub>4</sub>, together with the nitrogen atom to which R<sub>3</sub> and R<sub>4</sub> are attached, form piperidinyl.
3. The compound according to claim 2 which is (2R)-2-methyl-1-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-3-[thienophen-2-ylmethyl]-amino-propan-2-ol.
4. The compound according to claim 2 which is (2R)-2-methyl-1-[(pyridin-3-ylmethyl)-amino]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
5. The compound according to claim 2 which is (2R)-2-methyl-1-[(pyridin-2-ylmethyl)-amino]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
6. The compound according to claim 2 which is (2S)-1-(2-thienylmethylamino)-2-methyl-3-[3-thieno[2,3-d]isoxazol-3-yl-phenoxy]propan-2-ol.
- 30 7. The compound according to claim 2 which is (2S)-1-[4-(3-chlorophenoxy)-1-piperidinyl]-2-methyl-3-[3-thieno[2,3-d]isoxazol-3-yl-phenoxy]propan-2-ol.

8. The compound according to claim 2 which is (2S)-1-[4-(6-fluorobenzo[*d*]isoxazol-3-yl)piperidin-1-yl]-2-methyl-3-[3-thieno[2,3-*d*]isoxazol-3-yl-phenoxy]propan-2-ol.
9. The compound according to claim 2 which is (2R)-2-methyl-1-[(pyridin-4-ylmethyl)-amino]-3-(3-thieno[2,3-*d*]isoxazol-3-yl-phenoxy)propan-2-ol.
10. The compound according to claim 2 which is (2R)-1-[4-(6-fluorobenzo[*d*]isoxazol-3-yl)piperidin-1-yl]-3-(4-thieno[2,3-*d*]isoxazol-3-yl-phenoxy)propan-2-ol.
11. The compound according to claim 2 which is (2S)-1-(3-thienylmethylamino)-2-methyl-3-[3-thieno[2,3-*d*]isoxazol-3-yl-phenoxy]propan-2-ol.
12. The compound according to claim 2 which is (2S)-2-methyl-1-[(pyridin-3-ylmethyl)amino]-3-(3-thieno[2,3-*d*]isoxazol-3-yl-phenoxy)propan-2-ol.
13. The compound according to claim 2 which is (2S)-2-methyl-1-[(pyridin-2-ylmethyl)amino]-3-(3-thieno[2,3-*d*]isoxazol-3-yl-phenoxy)propan-2-ol.
14. The compound according to claim 2 which is (4-fluorophenyl)-(1-{2(R)-hydroxy-3-[3-(1-methyl-1H-thieno[3,2-*c*]pyrazol-3-yl)-phenoxy]-propyl}-piperidin-4-yl)-methanone.
15. The compound according to claim 2 which is 1-(1-{2(R)-hydroxy-3-[3-(1-methyl-1H-thieno[3,2-*c*]pyrazol-3-yl)-phenoxy]-propyl}-piperidin-4-yl)-1,3-dihydrobenzimidazol-2-one.
16. A compound according to claim 2 wherein  
R<sub>1</sub> is OH;  
R<sub>2</sub> is H;  
R<sub>3</sub> is (CH<sub>2</sub>)<sub>n</sub> Q; or  
R<sub>3</sub> and R<sub>4</sub> together with the nitrogen atom to which R<sub>3</sub> and R<sub>4</sub> are attached form piperidinyl; and  
n is 1.
17. A compound according to claim 16 wherein Q is thienyl.
18. The compound according to claim 17 which is (2R)-1-(4-thieno[2,3-*d*]isoxazol-3-yl-phenoxy)-3-[(thiophen-3-ylmethyl)-amino]-propan-2-ol.
19. The compound of claim 17 which is (2R)-1-(4-thieno[2,3-*d*]isoxazol-3-yl-phenoxy)-3-[(thiophen-2-ylmethyl)-amino]-propan-2-ol.

20. The compound of claim 17 which is (2R)-1-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-3-[(thiophen-2-ylmethyl)amino]propan-2-ol.
21. The compound of claim 17 which is (2R)-1-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-3-[(thiophen-3-ylmethyl)amino]propan-2-ol.
- 5 22. A compound according to claim 16 wherein Q is pyridyl.
23. The compound of claim 22 which is (2R)-1-[(pyridin-4-yl)methylamino]-3-[3-thieno[2,3-d]isoxazol-3-yl-phenoxy]propan-2-ol.
24. The compound of claim 22 which is (2R)-1-[(pyridin-2-ylmethyl)-amino]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
- 10 25. The compound of claim 22 which is (2R)-1-[(pyridin-3-ylmethyl)amino]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
26. A compound according to claim 16 wherein R<sub>3</sub> and R<sub>4</sub>, together with the nitrogen atom to which R<sub>3</sub> and R<sub>4</sub> are attached, form piperidinyl.
- 15 27. The compound according to claim 26 which is 4-(4-chlorophenyl)-1-{(R)2-hydroxy-3-[3-(thieno[2,3-d]isoxazol-3-yl)phenoxy]propyl}piperidin-4-ol.
28. The compound of claim 26 which is (2R)-1-[4-(6-fluorobenzo[d]isoxazol-3-yl)piperidin-1-yl]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
29. The compound of claim 26 which is (2R)-1-[4-(6-chlorobenzo[d]isoxazol-3-yl)piperidin-1-yl]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
- 20 30. The compound of claim 26 which is (2R)-1-[4-(6-fluorobenzo[d]isothiazol-3-yl)piperidin-1-yl]-3-(thieno[2,3-d]isoxazol-3-yl-phenoxy)propan-2-ol.
31. The compound of claim 26 which is (2R)-1-(4-benzylpiperidin-1-yl)-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
32. The compound of claim 26 which is (2R)-1-piperidin-1-yl-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
- 25 33. A compound according to claim 1 wherein R<sub>3</sub> and R<sub>4</sub>, together with the nitrogen atom to which R<sub>3</sub> and R<sub>4</sub> are attached, form piperazinyl.
34. The compound of claim 33 which is (2R)-1-[4-(4-chlorophenyl)piperazin-1-yl]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)propan-2-ol.
- 30 35. The compound of claim 33 which is (2R)-1-[4-(2-methoxyphenyl)-piperazin-1-yl]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.

36. The compound of claim 33 which is (2R)-1-[4-(2-fluorophenyl)piperazin-1-yl]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
37. The compound of claim 33 which is (2R)-1-[4-(4-fluorophenyl)piperazin-1-yl]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
- 5 38. The compound of claim 33 which is (2R)-1-[4-(2-chlorophenyl)piperazin-1-yl]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
39. The compound of claim 33 which is (2R)-1-[4-(3-chlorophenyl)piperazin-1-yl]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
40. The compound of claim 33 which is (2R)-1-[4-(4-methoxyphenyl)piperazin-1-yl]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
- 10 41. The compound of claim 33 which is (2R)-1-(4-phenylpiperazin-1-yl)-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)propan-2-ol.
42. The compound of claim 33 which is 2-{4-[(R)-2-hydroxy-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propyl]piperazin-1-yl}benzonitrile.
- 15 43. The compound of claim 33 which is (2R)-1-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-3-[4-(2-trifluoromethylphenyl)-piperazin-1-yl]propan-2-ol.
44. The compound of claim 33 which is (2R)-1-[4-(2-methoxyphenyl)piperazin-1-yl]-3-(4-thieno[2,3-d]isoxazol-3-yl-phenoxy)propan-2-ol.
45. The compound of claim 33 which is 2-{4-[(R)-2-hydroxy-3-(4-thieno[2,3-d]isoxazol-3-yl-phenoxy)propyl]piperazin-1-yl}benzonitrile.
- 20 46. The compound of claim 33 which is (2S)-1-[4-(2-methoxyphenyl)piperazin-1-yl]-2-methyl-3-[3-thieno[2,3-d]isoxazol-3-yl-phenoxy]propan-2-ol.
47. The compound of claim 33 which is (2S)-1-[4-(2-cyanophenyl)-1-piperazinyl]-2-methyl-3-[3-thieno[2,3-d]isoxazol-3-yl-phenoxy]propan-2-ol.
- 25 48. The compound of claim 33 which is (2R)-1-(4-pyrimidin-2-yl-piperazin-1-yl)-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
49. The compound of claim 33 which is (2R)-1-(4-pyridin-2-yl-piperazin-1-yl)-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
50. The compound of claim 33 which is (2R)-1-(4-benzo[1,3]dioxol-5-ylmethyl-30 piperazin-1-yl)-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)propan-2-ol.
51. The compound of claim 33 which is (2R)-1-[4-(6-fluoro-1H-indazol-3-yl)-piperazin-1-yl]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.

52. The compound of claim 33 which is (2R)-1-[4-(5-methoxy-1H-indazol-3-yl)-piperazin-1-yl]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
53. The compound of claim 33 which is (2R)-1-(4-benzo[d]isothiazol-3-yl-piperazin-1-yl)-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
- 5 54. The compound of claim 38 which is (2R)-1-[4-(6-fluorobenzo[b]thiophen-3-yl)piperazin-1-yl]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
55. The compound of claim 33 which is 3-((R)-4-[2-hydroxy-3(3-thieno[2,3-d]isoxazol-3-yl)phenoxy]propyl)-piperazin-1-yl]-benzo[d]isoxazol-6-ol.
- 10 56. The compound of claim 33 which is (2R)-1-[4-(4-methoxyphenyl)-3-methylpiperazin-1-yl]-3-[3-(thieno[2,3-d]isoxazol-3-yl)phenoxy]propan-2-ol.
57. The compound of claim 33 which is (2R)-1-[3-(1-methyl-1H-thieno[3,2-c]pyrazol-3-yl)-phenoxy-3-(4-phenyl-piperazin-1-yl)-propan-2-ol.
- 15 58. The compound of claim 33 which is (2R)-1-[3-(1-methyl-1H-thieno[3,2-c]pyrazol-3-yl)-phenoxy-3-(4-pyrimidin-2-yl-piperazin-1-yl)-propan-2-ol.
59. A compound according to claim 1 wherein Q is phenyl.
60. The compound of claim 59 which is (2R)-1-(4-chlorobenzylamino)-2-methyl-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
- 20 61. The compound of claim 59 which is (2R)-1-[(N-benzyl-N-methyl)amino]-3-[2-thieno[2,3-d]isoxazol-3-yl)phenoxy]-2-propanol.
62. The compound of claim 59 which is (2S)-(+)-1-benzylamino-2-methyl-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)propan-2-ol.
63. The compound of claim 59 which is (2R)-(-)-1-benzylamino-2-methyl-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)propan-2-ol.
- 25 64. The compound of claim 59 which is (2R)-1-(benzylmethylamino)-2-methyl-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)propan-2-ol.
65. The compound of claim 59 which is (2R)-1-(4-methoxybenzylamino)-2-methyl-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
66. The compound of claim 59 which is (2R)-1-(4-fluorobenzylamino)-2-methyl-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
- 30 67. The compound of claim 59 which is (2R)-1-(2-fluorobenzylamino)-2-methyl-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
68. The compound of claim 59 which is (2R)-2-methyl-1-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-3-(4-trifluoromethylbenzylamino)-propan-2-ol.

69. The compound of claim 59 which is (2R)-2-methyl-1-[1(R)-phenylethylamino]-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)-propan-2-ol.
70. The compound of claim 59 which is (2R)-2-methyl-1-[1(S)-phenylethylamino]-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)-propan-2-ol.
- 5 71. The compound of claim 59 which is (2R)-1-(2-hydroxy-2-phenylethylamino)-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)propan-2-ol.
72. The compound of claim 59 which is (2R)-benzyl-[2-methoxy-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)propyl]-methylamine hydrochloride.
- 10 73. The compound of claim 59 which is (2R)-benzyl-[2-methoxy-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)propyl]-amine.
74. The compound of claim 59 which is (2S)-1-(4-fluorobenzylamino)-2-methyl-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)propan-2-ol.
- 15 75. The compound of claim 59 which is (2S)-1-(2-fluorobenzylamino)-2-methyl-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)propan-2-ol.
76. The compound of claim 59 which is (2S)-1-(3-fluorobenzylamino)-2-methyl-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)propan-2-ol.
- 20 77. The compound of claim 59 which is (2S)-1-(4-chlorobenzylamino)-2-methyl-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)propan-2-ol.
78. The compound of claim 59 which is (2S)-1-(2-chlorobenzylamino)-2-methyl-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)propan-2-ol.
- 25 79. The compound of claim 59 which is (2S)-1-(3,4-dichlorobenzylamino)-2-methyl-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)propan-2-ol.
80. The compound of claim 59 which is (2S)-2-methyl-1-[1(R)-phenylethylamino]-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)-propan-2-ol.
- 25 81. The compound of claim 59 which is (2S)-2-methyl-1-[1(S)-phenylethylamino]-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)-propan-2-ol.
82. The compound of claim 59 which is (2S)-2-methyl-1-(4-methylbenzylamino)-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)propan-2-ol.
- 30 83. The compound of claim 59 which is (2S)-1-(4-methoxybenzylamino)-2-methyl-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)propan-2-ol.
84. The compound of claim 59 which is (2S)-1-(2-methoxybenzylamino)-2-methyl-3-(3-thieno[2,3-d]isoxazol]-3-yl-phenoxy)propan-2-ol.

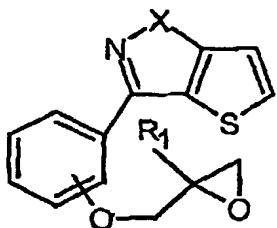
85. The compound of claim 59 which is (2S)-1-(benzylmethylamino)-2-methyl-3-[3-thieno[2,3-d]isoxazol-3-yl-phenoxy]propan-2-ol.
86. The compound of claim 59 which is (2S)-1-(3,4-difluorobenzylamino)-2-methyl-3-[3-(thieno[2,3-d]isoxazol-3-yl)phenoxy]propan-2-ol.
87. The compound of claim 59 which is (2R)-1-(2-methoxybenzylamino)-2-methyl-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
88. A compound according to claim 1 wherein Q is furanyl.
89. The compound of claim 88 which is (2R)-1-[(furan-2-ylmethyl)-amino]-2-methyl-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
90. The compound of claim 88 which is (2R)-1-[(furan-2-ylmethyl)amino]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
91. The compound of claim 88 which is (2R)-1-[(furan-2-ylmethyl)-amino]-3-(4-thieno[2,3-d]isoxazol-3-yl-phenoxy)propan-2-ol.
92. The compound of claim 88 which is (2S)-1-[(furan-2-ylmethyl)amino]-2-methyl-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)propan-2-ol.
93. A compound according to claim 1 wherein R<sub>3</sub> is indanyl.
94. The compound of claim 93 which is (2R)-1-(indan-1-ylamino)-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
95. The compound of claim 93 which is (2R)-1-(indan-2-ylamino)-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
96. A compound according to claim 1 wherein Q is naphthyl.
97. The compound of claim 96 which is (2R)-1-[(naphthalen-1-ylmethyl)amino]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)propan-2-ol.
98. The compound of claim 96 which is (2R)-2-methyl-1-[(naphthalen-1-ylmethyl)amino]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
99. The compound of claim 96 which is (2R)-1-[(naphthalen-1-ylmethyl)-amino]-3-(4-thieno[2,3-d]isoxazol-3-yl-phenoxy)-propan-2-ol.
100. The compound of claim 96 which is (2S)-2-methyl-1-[(naphthalen-1-ylmethyl)amino]-3-(3-thieno[2,3-d]isoxazol-3-yl-phenoxy)propan-2-ol.
101. A compound according to claim 1 wherein R<sub>3</sub> and R<sub>4</sub>, together with the nitrogen atom to which R<sub>3</sub> and R<sub>4</sub> are attached, form 1,2,3,4-tetrahydroisoquinolinyl.

102. The compound of claim 101 which is is ( $\pm$ )-1-(3,4-dihydro-1H-isoquinolin-2-yl)-3-[2-(thieno[2,3-*d*]isoxazol-3-yl)phenoxy]-2-propanol.
103. The compound of claim 101 which is (2*R*)-1-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-yl)-3-[3-(thieno[2,3-*d*]isoxazol-3-yl)phenoxy]propan-2-ol.
104. The compound of claim 101 which is (2*R*)-1-(3,4-dihydro-1H-isoquinolin-2-yl)-3-[2-(thieno[2,3-*d*]isoxazol-3-yl)phenoxy]-2-propanol.
105. The compound of claim 101, which is (2*R*)-1-(3,4-dihydro-1H-isoquinolin-2-yl)-3-[3-(1-methyl-1H-thieno[3,2-*c*]pyrazol-3-yl)-phenoxy]-propan-2-ol.
106. A compound according to claim 1, wherein R<sub>3</sub> and R<sub>4</sub>, together with the nitrogen atom to which R<sub>3</sub> and R<sub>4</sub> are attached, form 1,2,3,4-tetrahydro- $\beta$ -carbolinyl.
107. The compound of claim 106 which is (2*R*)-1-(1,2,3,4-tetrahydro- $\beta$ -carbolin-2-yl)-3-[3-thieno[2,3-*d*]isoxazol-3-yl)phenoxy]propan-2-ol.
108. A compound according to claim 1, wherein R<sub>3</sub> and R<sub>4</sub>, together with the nitrogen atom to which R<sub>3</sub> and R<sub>4</sub> are attached, form 4,5,6,7-tetrahydrothieno[3,2-*c*]pyridinyl.
109. The compound of claim 108 which is (2*R*)-1-(6,7-dihydro-4H-thieno[3,2-*c*]pyridin-5-yl)-3-(3-thieno[2,3-*d*]isoxazol-3-yl-phenoxy)propan-2-ol.
110. The compound of claim 108 which is (2*R*)-1-(6,7-dihydro-4H-thieno[3,2-*c*]pyridin-5-yl)-3-(4-thieno[2,3-*d*]isoxazol-3-yl-phenoxy)propan-2-ol.
111. A compound according to claim 1, wherein R<sub>3</sub> and R<sub>4</sub>, together with the nitrogen atom to which R<sub>3</sub> and R<sub>4</sub> are attached, form 8-aza-bicyclo[3.2.1.]octane.
112. The compound of claim 111 which is (2*R*)-1-(3-benzo[*d*]isoxazol-3-yl-8-azabicyclo[3.2.1]oct-8-yl-3-(3-thieno[2,3-*d*]isoxazol-3-yl-phenoxy)propan-2-ol.
113. A compound according to claim 1, wherein R<sub>3</sub> is adamantyl.
114. The compound of claim 113 which is (2*R*)-1-(adamantan-1-ylamino)-3-(3-thieno[2,3-*d*]isoxazol-3-yl-phenoxy)-propan-2-ol.
115. A compound according to claim 1, wherein Q is cyclohexyl.
116. compound of claim 115 which is (2*R*)-1-(cyclohexylmethyl-amino)-3-(3-thieno[2,3-*d*]isoxazol-3-yl-phenoxy)-propan-2-ol.
117. A compound according to claim 1, wherein Q is benzimidazolyl.

PART 34 AMENDMENT

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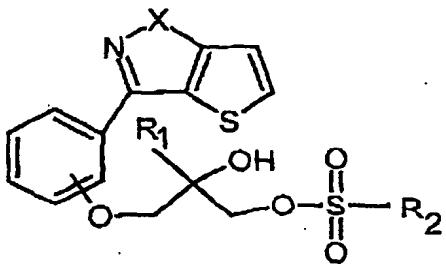
118. The compound of claim 117 which is (2R)-1-[(1H-benzimidazol-2-ylmethyl)amino]-3-[3-thieno[2,3-d]isoxazol-3-yl-phenoxy]propan-2-ol.
119. A compound according to claim 1, wherein R<sub>3</sub> is 1,2,3,4-tetrahydronaphthyl.
120. The compound of claim 119 which is (2R)-1-(1,2,3,4-tetrahydronaphthalen-1-ylamino)-3-[3-thieno[2,3-d]isoxazol-3-yl]phenoxy]propan-2-ol.
121. A compound of formula



wherein X is N(CH<sub>3</sub>) or O; and

R<sub>1</sub> is C<sub>1-6</sub>alkyl.

122. A compound of formula



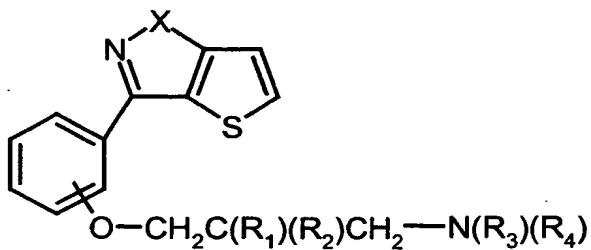
wherein X is N(CH<sub>3</sub>) or O;

R<sub>1</sub> is H or C<sub>1-6</sub>alkyl; and

R<sub>2</sub> is CH<sub>3</sub>, F, p-bromobenzene, p-nitrobenzene, or p-methylbenzene.

123. A method for antagonizing the effects of dopamine at the D<sub>4</sub> receptor comprising administering a compound according to claim 1 to a patient in need thereof.
124. A composition comprising a compound according to claim 1 in admixture with an inert carrier.
125. The composition according to claim 124, wherein said inert carrier is a pharmaceutical carrier.
126. A method of treating psychoses comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to claim 1.

127. A method of treating Attention Deficit Hyperactivity Disorder comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to claim 1.
128. A method of treating Obsessive-Compulsive Disorder comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to claim 1.
129. A method of treating Substance Abuse comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to claim 1.
- 10 130. A method of treating Substance Dependence comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to claim 1.
131. A method of treating Parkinson's Disease comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to claim 1.
- 15 132. A method of treating Parkinsonism comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to claim 1.
133. A method of treating Tardive Dyskinesia comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to claim 1.
- 20 134. A method of treating Gilles de la Tourette Syndrome comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to claim 1.
135. A method of treating Conduct Disorder comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to claim 1.
- 25 136. A method of treating Oppositional Defiant Disorder comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to claim 1.
- 30 137. A method of making a compound of formula I



a pharmaceutically acceptable salt or stereoisomer thereof,

wherein

X is N(CH<sub>3</sub>) or O;

5 R<sub>1</sub> is OH or C<sub>1-6</sub> alkoxy;

R<sub>2</sub> is H or C<sub>1-6</sub> alkyl;

R<sub>3</sub> is (CH<sub>2</sub>)<sub>n</sub>Q, CH<sub>2</sub>CH(OH)Q, CH(CH<sub>3</sub>)Q, 1,2,3,4-tetrahydronaphthyl, indanyl, or adamantlyl, wherein

Q is thienyl, phenyl, furanyl, naphthyl, pyridyl, indolyl, indazolyl,

10 cyclohexyl, 1,2-methylenedioxyphenyl, cyclohexenyl, 1H-pyrazolo[4,3-c]pyridyl, and

Q is optionally substituted with one or two moieties independently:

selected from halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, hydroxy, S(O)<sub>2</sub>NH<sub>2</sub>, trifluoromethyl, or cyano, and

15 n is 1 or 2;

R<sub>4</sub> is H or C<sub>1-6</sub> alkyl; or

R<sub>3</sub> and R<sub>4</sub>, together with the nitrogen atom to which R<sub>3</sub> and R<sub>4</sub> are attached, form

20 1,4-dioxa-8-azo-spiro[4.5]decanyl, piperazinyl, morpholinyl, piperidinyl, pyrrolidinyl, azocanyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydro-β-carbolinyl, 4,5,6,7-tetrahydrothienyl[3,2-c]pyridyl, or 8-aza-

bicyclo[3.2.1.]octane, each of which may be mono- or independently disubstituted with halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, C(O)phenyl, OH, CN, O-phenyl or (CH<sub>2</sub>)<sub>m</sub>Z,

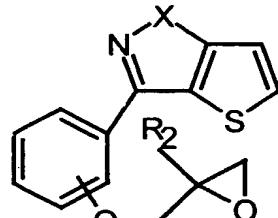
-149-

Z is benzisoxazolyl, indazolyl, benzisothiazolyl, benzothienyl, pyrimidinyl, pyridyl, 1,2-methylenedioxyphenyl, or phenyl, and

5 Z, CH(OH)phenyl or O-phenyl are optionally substituted with one or two moieties independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, hydroxy, trifluoromethyl, S(O)<sub>2</sub>NH<sub>2</sub>, or cyano, and

10 m is 0 or 1;

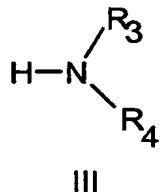
comprising the step of coupling a reagent of formula II



II

15

wherein X and R<sub>2</sub> are as defined in formula I;  
with a reagent of formula III

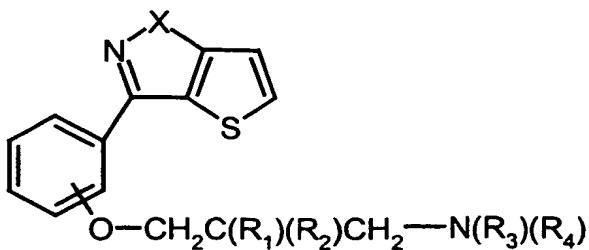


III

wherein R<sub>3</sub> and R<sub>4</sub> are as defined in formula I;

20 to provide the compound of formula I.

138. A method of making a compound of formula I



|

a pharmaceutically acceptable salt or stereoisomer thereof,  
wherein

X is N(CH<sub>3</sub>) or O;

5 R<sub>1</sub> is OH or C<sub>1-6</sub> alkoxy;

R<sub>2</sub> is H or C<sub>1-6</sub> alkyl;

10 R<sub>3</sub> is (CH<sub>2</sub>)<sub>n</sub> Q, CH<sub>2</sub>CH(OH)Q, CH(CH<sub>3</sub>)Q, 1,2,3,4-tetrahydronaphthyl, indanyl, or adamanyl, wherein

Q is thienyl, phenyl, furanyl, naphthyl, pyridyl, indolyl, indazolyl,

15 cyclohexyl, 1,2-methylenedioxyphenyl, cyclohexenyl, 1H-pyrazolo[4,3-c]pyridyl, and

Q is optionally substituted with one or two moieties independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, hydroxy, S(O)<sub>2</sub>NH<sub>2</sub>, trifluoromethyl, or cyano, and

20 n is 1 or 2;

R<sub>4</sub> is H or C<sub>1-6</sub> alkyl; or

25 R<sub>3</sub> and R<sub>4</sub>, together with the nitrogen atom to which R<sub>3</sub> and R<sub>4</sub> are attached, form 1,4-dioxa-8-azo-spiro[4.5]decanyl, piperazinyl, morpholinyl, piperidinyl, pyrrolidinyl, azocanyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydro-β-carbolinyl, 4,5,6,7-tetrahydrothienyl[3,2-c]pyridyl, or 8-aza-bicyclo[3.2.1.]octane, each of which may be mono- or independently disubstituted with halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, C(O)phenyl, OH, CN, O-phenyl or (CH<sub>2</sub>)<sub>m</sub>Z,

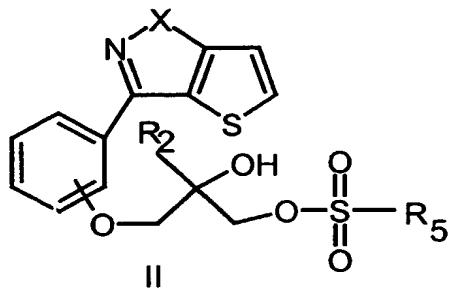
-151-

Z is benzisoxazolyl, indazolyl, benzisothiazolyl, benzothienyl, pyrimidinyl, pyridyl, 1,2-methylenedioxyphenyl, or phenyl, and

5 Z, CH(OH)phenyl or O-phenyl are optionally substituted with one or two moieties independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, hydroxy, trifluoromethyl, S(O)<sub>2</sub>NH<sub>2</sub>, or cyano, and

10 m is 0 or 1;

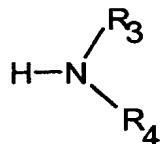
comprising the step of coupling a compound of formula II



wherein X and R<sub>2</sub> are as defined in formula I; and

15 R<sub>5</sub> is CH<sub>3</sub>, CF<sub>3</sub>, F, p-bromobenzene, p-nitrobenzene, or p-methylbenzene;

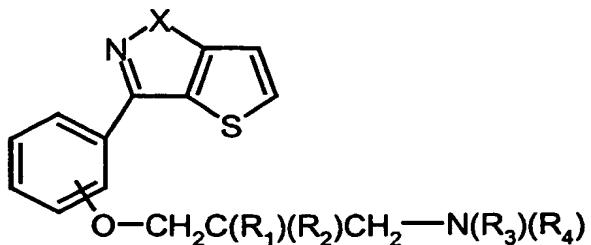
with a reagent of formula III



wherein R<sub>3</sub> and R<sub>4</sub> are as defined in formula I;

to provide the compound of formula I.

20 139. A method of making a compound of formula I



a pharmaceutically acceptable salt or stereoisomer thereof,  
wherein

X is N(CH<sub>3</sub>) or O;

R<sub>1</sub> is OH or C<sub>1-6</sub> alkoxy;

R<sub>2</sub> is H or C<sub>1-6</sub> alkyl;

R<sub>3</sub> is (CH<sub>2</sub>)<sub>n</sub> Q, CH<sub>2</sub>CH(OH)Q, CH(CH<sub>3</sub>)Q, 1,2,3,4-tetrahydronaphthyl, indanyl, or adamanyl, wherein

Q is thienyl, phenyl, furanyl, naphthyl, pyridyl, indolyl, indazolyl, cyclohexyl, 1,2-methylenedioxyphenyl, cyclohexenyl, 1H-pyrazolo[4,3-c]pyridyl, and

10 Q is optionally substituted with one or two moieties independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, hydroxy, S(O)<sub>2</sub>NH<sub>2</sub>, trifluoromethyl, or cyano, and

n is 1 or 2;

15 R<sub>4</sub> is H or C<sub>1-6</sub> alkyl; or

R<sub>3</sub> and R<sub>4</sub>, together with the nitrogen atom to which R<sub>3</sub> and R<sub>4</sub> are attached, form 1,4-dioxa-8-azo-spiro[4.5]decanyl, piperazinyl, morpholinyl, piperidinyl, 20 pyrrolidinyl, azocanyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydro-β-carbolinyl, 4,5,6,7-tetrahydrothienyl[3,2-c]pyridyl, or 8-aza-bicyclo[3.2.1.]octane, each of which may be mono- or independently disubstituted with halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, C(O)phenyl, OH, CN, O-phenyl or (CH<sub>2</sub>)<sub>m</sub>Z,

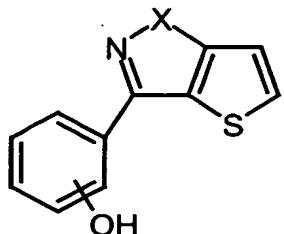
25 Z is benzisoxazolyl, indazolyl, benzisothiazolyl, benzothienyl, pyrimidinyl, pyridyl, 1,2-methylenedioxyphenyl, or phenyl, and

30 Z, CH(OH)phenyl or O-phenyl are optionally substituted with one or two moieties independently selected from halo, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, hydroxy, trifluoromethyl, S(O)<sub>2</sub>NH<sub>2</sub>, or cyano, and

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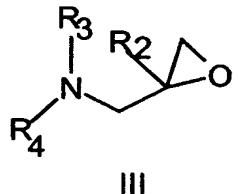
m is 0 or 1;

comprising the step of coupling a reagent of formula II



5 wherein X is as defined in formula I;

with a reagent of formula III



wherein R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub> are as defined in formula I;

to provide the compound of formula I.

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